

1600

RAW SEQUENCE LISTING

PATENT APPLICATION: US/09/618,380B

DATE: 09/22/2003 TIME: 11:06:09 7

Input Set : A:\058820176CNUS03.txt

Output Set: N:\CRF4\09222003\I618380B.raw

```
3 <110> APPLICANT: Weiner, George
        Gingrich, Roger
 5
        Link, Brian
        Tso, J. Yun
 8 <120> TITLE OF INVENTION: HUMANIZED ANTIBODIES AGAINST CD3
10 <130> FILE REFERENCE: 05882-0176-CNUS03
12 <140> CURRENT APPLICATION NUMBER: US 09/618,380B
13 <141> CURRENT FILING DATE: 2000-07-18
15 <150> PRIOR APPLICATION NUMBER: US 08/397,411
16 <151> PRIOR FILING DATE: 1995-03-01
18 <150> PRIOR APPLICATION NUMBER: US 07/859,583
19 <151> PRIOR FILING DATE: 1992-03-27
21 <160> NUMBER OF SEQ ID NOS: 14
23 <170> SOFTWARE: PatentIn version 3.1
25 <210> SEQ ID NO: 1
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27 <212> TYPE: PRT
28 <213> ORGANISM: Artificial Sequence
30 <220> FEATURE:
31 <223> OTHER INFORMATION: Light chain of Humanized 1D10 Ab minus signal sequence
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39 Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Glu Asn Ile Tyr Ser Tyr
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                                   25
43 Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Val
                               40
47 Ser Asn Ala Lys Thr Leu Ala Glu Gly Val Pro Ser Arg Phe Ser Gly
51 Ser Gly Ser Gly Lys Gln Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
                                           75
                       70
55 Glu Asp Phe Ala Thr Tyr Tyr Cys Gln His His Tyr Gly Asn Ser Tyr
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70 Asp Ile Gln Met Thr Gln Ser Pro Ala Ser Leu Ser Ala Ser Val Gly

74 Glu Thr Val Thr Ile Thr Cys Arg Ala Ser Glu Asn Ile Tyr Ser Tyr

63 <210> SEQ ID NO: 2 64 <211> LENGTH: 107 65 <212> TYPE: PRT

68 <400> SEQUENCE: 2

66 <213> ORGANISM: Mus sp.

60

56 85 90 59 Pro Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys

5

100



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```
75
              20
                                  25
78 Leu Ala Trp Tyr Gln Gln Lys Gln Gly Lys Ser Pro Gln Leu Leu Val
82 Ser Asn Ala Lys Thr Leu Ala Glu Gly Val Thr Ser Arg Phe Ser Gly
86 Ser Gly Ser Gly Lys Gln Phe Ser Leu Lys Ile Asn Ser Leu Gln Pro
                      70
                                          75
90 Glu Asp Phe Gly Asn Tyr Tyr Cys Gln His His Tyr Gly Asn Ser Tyr
                                      90
94 Pro Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
              100
98 <210> SEQ ID NO: 3
99 <211> LENGTH: 116
100 <212> TYPE: PRT
101 <213> ORGANISM: Artificial Sequence
103 <220> FEATURE:
104 <223> OTHER INFORMATION: Heavy chain of Humanized 1D10 Ab minus signal sequence
106 <400> SEQUENCE: 3
108 Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
112 Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Phe Ser Leu Thr Asn Tyr
     20
                                   25
116 Gly Val His Trp Val Arg Gln Ser Pro Gly Lys Gly Leu Glu Trp Ile
                               40
120 Gly Val Lys Trp Ser Gly Gly Ser Thr Glu Tyr Asn Ala Ala Phe Ile
           55
124 Ser Arg Leu Thr Ile Ser Lys Asp Thr Ser Lys Asn Gln Val Ser Leu
128 Lys Leu Asn Ser Leu Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
       85
                                       90
132 Arg Asn Asp Arg Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu Val
136 Thr Val Ser Ser
          115
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143 <213> ORGANISM: Mus sp.
145 <400> SEQUENCE: 4
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155 Gly Val His Trp Val Arg Gln Ser Pro Gly Lys Gly Leu Glu Trp Leu
159 Gly Val Lys Trp Ser Gly Gly Ser Thr Glu Tyr Asn Ala Ala Phe Ile
                           55
163 Ser Arg Leu Ser Ile Ser Lys Asp Asn Ser Lys Ser Gln Val Phe Phe
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164 65



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167 Lys Met Asn Ser Leu Gln Ala Asp. Asp Thr Ala Met Tyr Tyr Cys Ala 85 90 171 Arg Asn Asp Arg Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Ser Val 172 100 105 175 Thr Val Ser Ser 176 115 179 <210> SEQ ID NO: 5 180 <211> LENGTH: 214 181 <212> TYPE: PRT 182 <213> ORGANISM: Artificial Sequence 184 <220> FEATURE: . 185 <223> OTHER INFORMATION: Complete light chain of Humanized 1D10 Ab 187 <400> SEQUENCE: 5 189 Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly 193 Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Glu Asn Ile Tyr Ser Tyr 197 Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Val 198 35 40 201 Ser Asn Ala Lys Thr Leu Ala Glu Gly Val Pro Ser Arg Phe Ser Gly 55 205 Ser Gly Ser Gly Lys Gln Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro 206 65 70 75 209 Glu Asp Phe Ala Thr Tyr Tyr Cys Gln His His Tyr Gly Asn Ser Tyr 213 Pro Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala Ala 214 100 217 Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly 218 115 120 221 Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala 130 135 140 225 Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln 150 155 229 Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser 165 170 233 Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr 180 185 190 237 Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser 195 200 205 241 Phe Asn Arg Gly Glu Cys 210 245 <210> SEQ ID NO: 6 246 <211> LENGTH: 273 247 <212> TYPE: PRT 248 <213> ORGANISM: Artificial Sequence 250 <220> FEATURE: 251 <223> OTHER INFORMATION: Fd-jun in F(ab'-zipper)2 of humanized 1D10 antibody 253 <400> SEQUENCE: 6

255 Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu 🕑



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Input Set : A:\058820176CNUS03.txt
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256	1	L 5 .							10					15		
259	Thr	Leu	Ser	Leu	Thr	Cys	Thr	Val	Ser	Gly	Phe	Ser	Leu	Thr	Asn	Tyr
260				20		-			25	-				30		-
263	Gly	Val	His	Trp	Val	Arq	Gln	Ser	Pro	Gly	Lys	Gly	Leu	Glu	Trp	Ile
264	-		35	-		_		40		_	-	_	45		_	
267	Gly	Val	Lvs	Trp	Ser	Glv	Gly	Ser	Thr	Glu	Tyr	Asn	Ala	Ala	Phe	Ile
268	-	50	_	•		-	55			٠	•	60				
271	Ser	Ara	Leu	Thr	Ile	Ser	Lvs	Asp	Thr	Ser	Lvs	Asn	Gln	Val	Ser	Leu
272						70	-	. •			75					80
		Leu	Asn	Ser	Leu	Thr	Ala	Ala	qaA	Thr	Ala	Val	Tvr	Tvr	Cvs	Ala
276	-2				85				•	90	•		-		95	
	Arq	Asn	Asp	Arq	Tyr	Ala	Met	Asp	Tyr	Trp	Gly	Gln	Gly	Thr	Leu	Val
280	,		-	100	-			•	105	•	-			110		
283	Thr	Val	Ser	Ser	Ala	Ser	Thr	Lys	Gly	Pro	Ser	Val	Phe	Pro	Leu	Ala
284			115					120	-				125			
	Pro	Ser	Ser	Lys	Ser	Thr	Ser	Gly	Gly	Thr	Ala	Ala	Leu	Gly	Cys	Leu
288		130		-			135	•	-			140		-	-	
291	Val	Lys	Asp	Tyr	Phe	Pro	Glu	Pro	Val	Thr	Val	Ser	Trp	Asn	Ser	Gly
	145	-	-	-		150					155		-			160
295	Ala	Leu	Thr	Ser	Gly	Val	His	Thr	Phe	Pro	Ala	Val	Leu	Gln	Ser	Ser
296					165					170					175	
299	Gly	Leu	Tyr	Ser	Leu	Ser	Ser	Val	Val	Thr	Val	Pro	Ser	Ser	Ser	Leu
300	-			180					185					190		
303	Gly	Thr	Gln	Thr	Tyr	Ile	Cys	Asn	Val	Asn	His	Lys	Pro	Ser	Asn	Thr
304	_		195					200					205			
307	Lys	Val	Asp	Lys	Lys	Val	Glu	Pro	Lys	Ser	Cys	Asp	Lys	Thr	His	Thr
308		210					215					220				
311	Cys	Pro	Pro	Cys	Lys	Cys	Pro	Ala	Gly	Gly	Arg	Ile	Ala	Arg	Leu	Glu
312	225					230					235					240
315	Glu	Lys	Val	Lys	Thr	Leu	Lys	Ala	Gln	Asn	Ser	Glu	Leu	Ala	Ser	Thr
316					245					250					255	
319	Ala	Asn	Met	Leu	Arg	Glu	Gln	Val	Ala	Gln	Leu	Lys	Gln	Lys	Val	Met _.
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323	Asn															
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			EATU													
333	3 <223> OTHER INFORMATION: Complete heavy chain of Humanized 1D10 Ab															
			EQUE													
337	Gln	Val	Gln	Leu	Gln	Glu	Ser	Gly	Pro	Gly	Leu	Val	Lys	Pro	Ser	Glu
338					5					10					15	
	Thr	Leu	Ser	Leu	Thr	Cys	Thr	Val		Gly	Phe	Ser	Leu		Asn	Tyr
342				20					25					30		
	Gly	Val		Trp	Val	Arg	Gln	Ser	Pro	Gly	Lys	Gly		Glu	Trp	Ile
346			<u>3</u> 5					40					45			_
	Gly		Lys	Trp	Ser	Gly		Ser	Thr	Glu	Tyr		Ala	Ala	Phe	Ile
350		50					55					60				



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353 354		Arg	Leu	Thr	Ile	Ser 70	Lys	Asp.	Thr	Ser	Lys 75	Asn	Gln	Val	Ser	Leu 80
		Len	Asn	Ser	Len	_	Ala	Ala	Asp	Thr	_	Val	Tvr	Tyr	Cvs	
358	2,5	cu	11011	501	85	****	1110	1110	пор	90			- 1 -	-]	95	
	Ara	Asn	Asn	Ara		Ala	Met	Asp	Tur		Glv	Gln	Glv	Thr		Val
362	9		1101	100	- 1 -			1100	105		027	01		110		
	Thr	Val	Ser		Ala	Ser	Thr	Lvs		Pro	Ser	Val	Phe	Pro	Len	Ala
366		, u i	115	DCL	1114	001		120	011		001		125		200	
	Pro	Ser		Lvs	Ser	Thr	Ser		Glv	Thr	Ala	Ala	_	Gly	Cvs	Leu
370		130	552				135	0-1	0 -1			140		1	- 3 -	
	Val		Asp	Tvr	Phe	Pro		Pro	Val	Thr	Val		Trp	Asn	Ser	Glv
	145	-1-		-1-		150					155		-			160
		Leu	Thr	Ser	Glv		His	Thr	Phe	Pro	Ala	Val	Leu	Gln	Ser	Ser
378					165					170					175	
	Glv	Leu	Tvr	Ser	Leu	Ser	Ser	Val	Val	Thr	Val	Pro	Ser	Ser	Ser	Leu
382	_		2	180					185					190		
385	Gly	Thr	Gln	Thr	Tyr	Ile	Cys	Asn	Val	Asn	His	Lys	Pro	Ser	Asn	Thr
386	-		195		-		•	200				-	205			
389	Lys	Val	Asp	Lys	Lys	Val	Glu	Pro	Lys	Ser	Cys	Asp	Lys	Thr	His	Thr
390		210		- ,			215					220				
393	Cys	Pro	Pro	Cys	Pro	Ala	Pro	Glu	Leu	Leu	Gly	Gly	Pro	Ser	Val	Phe
394	225					230		•			235					240
397	Leu	Phe	Pro	Pro	Lys	Pro	Lys	Asp	Thr	Leu	Met	Ile	Ser	Arg	Thr	Pro
398					245					250					255	
401	Glu	Val	Thr	Cys	Val	Val	Val	Asp	Val	Ser	His	Glu	Asp	Pro	Glu	Val
402				260					265		_			270		
	Lys	Phe		Trp	Tyr	Val	Asp	_	Val	Glu	Val	His		Ala	Lys	Thr
406	_	_	275				_	280	_		_	_	285		_	
	Lys		Arg	GIu	GLu	Gin		Asn	Ser	Thr	Tyr		vaı	Val	Ser	vaı
410	.	290	** - 1	T	11.2 -	C3	295	m	т	70	C1	300	C1	m	T	C
		Tnr	vaı	ьeu	HIS	310	Asp	Trp	Leu	Asn	315	ьуѕ	GIU	Tyr	глх	320
	305	Wa I	C02	Nan	T 1/0		T 011	Dro	·7\ 1 ~	Dro		Clu	Tvc	Thr	Tlo	
417	гу	vai	ser	ASII	325	ніа	ьеи	PIO	Ата	330	116	GIU	пуз	1111	335	Ser
	Luc	Δla	Luc	Glv		Pro	Δra	Glu	Pro		Va 1	Tur	Thr	Leu		Pro
422	цуз	лта	цуз	340	0111	110	1119	OIU	345	OIII	VUI	- y -		350	110	110
	Ser	Ara	Asp		Leu	Thr	Lvs	Asn		Val	Ser	Leu	Thr	Cys	Leu	Val
426	JUL	9	355	0_4				360	0				365	-1-		
	Lvs	Glv		Tvr	Pro	Ser	Asp		Ala	Val	Glu	Trp	Glu	Ser	Asn	Gly
430	-1-	370		- 4 -			375					380				•
	Gln	Pro	Glu	Asn	Asn	Tyr		Thr	Thr	Pro	Pro	_	Leu	Asp	Ser	Asp
	385					390	-				395			-		400
437	Gly	Ser	Phe	Phe	Leu	Tyr	Ser	Lys	Leu	Thr	Val	Asp	Lys	Ser	Arg	Trp
438	_				405					410					415	
441	Gln	Gln	Gly	Asn	Val	Phe	Ser	Cys	Ser	·Val	Met	His	Glu	Ala	Leu	His
442				420					425					430		
445	Asn	His	Tyr	Thr	Gln	Lys	Ser	Leu	Ser	Leu	Ser	Pro	Gly	Lys		
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RAW SEQUENCE LISTING ERROR SUMMARY PATENT APPLICATION: US/09/618,380B

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Please Note:

Use of n and/or Xaa have been detected in the Sequence Listing. Please review the Sequence Listing to ensure that a corresponding explanation is presented in the <220> to <223> fields of each sequence which presents at least one n or Xaa.

Seq#:14; Xaa Pos. 2,3,4,5,6,7